PROCESSING COMPLETED FOR L32
L33 3 DUP REM L32 (7 DUPLICATES REMOVED)

=> d l33 1-3 ibib abs

L33 ANSWER 1 OF 3 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 1
ACCESSION NUMBER: 2000442671 EMBASE
TITLE: .beta.-Amyloid-induced migration of monocytes across human brain endothelial cells involves **RAGE** and PECAM-1.
AUTHOR: Giri R.; Shen Y.; Stins M.; Yan S.D.; Schmidt A.M.; Stern D.; Kim K.-S.; **Zlokovic B.**; Kalra V.K.
CORPORATE SOURCE: V.K. Kalra, HMR 611, Dept. of Biochem./Molecular Biol., USC Keck School of Medicine, Los Angeles, CA 90033, United States. vkalra@hsc.usc.edu
SOURCE: American Journal of Physiology - Cell Physiology, (2000) 279/6 48-6 (C1772-C1781).
Refs: 30
ISSN: 0363-6143 CODEN: AJPCDD
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In patients with amyloid .beta.-related cerebrovascular disorders, e.g., Alzheimer's disease, one finds increased deposition of amyloid peptide (A.beta.) and increased presence of monocyte/microglia cells in the brain.
However, relatively little is known of the role of A.beta. in the trafficking of monocytes across the blood-brain barrier (BBB). Our studies show that interaction of A.beta.(1-40) with monolayer of human brain endothelial cells results in augmented adhesion and transendothelial migration of monocytic cells (THP-1 and HL-60) and peripheral blood monocytes. The A.beta.-mediated migration of monocytes was **inhibited** by antibody to A.beta. receptor (**RAGE**) and platelet endothelial cell adhesion molecule (PECAM-1). Additionally, A.beta.-induced transendothelial migration of monocytes were **inhibited** by protein kinase C **inhibitor** and augmented by phosphatase **inhibitor**. We conclude that interaction of A.beta. with **RAGE** expressed on brain endothelial cells initiates cellular signaling leading to the transendothelial migration of monocytes. We suggest that increased diapedesis of monocytes across the BBB in response to A.beta. present either in the peripheral circulation or in the brain parenchyma may play a role in the pathophysiology of A.beta.-related vascular disorder.

L33 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:134939 BIOSIS
DOCUMENT NUMBER: PREV200100134939
TITLE: Effect of endothelial cell polarity on Abeta-induced migration of monocytes across cultured brain endothelial cell monolayers of normal and AD individuals.
AUTHOR(S): Kalra, V. K. (1); Stins, M. A.; Kim, K. S.; Miller, C. A.; Yan, S. D.; Schmidt, A. M.; Stern, D. M.; Tokes, Z. A.; **Zlokovic, B. V.**; Giri, R.
CORPORATE SOURCE: (1) University of Southern California, Los Angeles, CA USA
SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-859.2. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience
. ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In patients with amyloid beta-related cerebrovascular disorders one finds increased deposition of amyloid peptide (Abeta) as well as increased presence of monocytes in the brain. However, relatively little is known of the role of Abeta in trafficking of blood monocytes across the blood brain barrier and concomitant accumulation of monocytes/ microglia in AD brain.
Our studies show that Abeta(1-40)- mediates transmigration of peripheral blood monocytes, HL-60 and THP-1 monocytic cells across monolayer of brain endothelial cells (BEC) derived from normal and AD individuals. The Abeta-induced transmigration of monocytes was > 75% **inhibited** by antibodies to Abeta-putative receptor **RAGE** and PECAM-1. The transmigration of monocytes across monolayer of BEC cultivated in Transwell chamber was apprx1.7 fold more when Abeta was added to the bottom (abluminal) side of AD vs normal individual BEC (n=3). The transmigration of monocytes was **inhibited** by tyrosine kinase and protein kinase C **inhibitors**, and augmented by protein phosphatase **inhibitor**. Our studies show that Abeta causes time dependent increase in the phosphorylation of PECAM-1 at tyrosine residues.
We conclude that (i) interaction of Abeta with **RAGE** on BEC initiates cellular signaling leading to the phosphorylation of PECAM-1, which may have a direct or causal effect on the trafficking of monocytes, and (ii) there is a differential response to Abeta when added to abluminal side of AD vs normal BEC monolayer.

L33 ANSWER 3 OF 3 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 2
ACCESSION NUMBER: 1998293065 EMBASE
TITLE: Human blood-brain barrier receptors for Alzheimer's amyloid-.beta. 1-40. Asymmetrical binding, endocytosis, and transcytosis at the apical side of brain microvascular endothelial cell monolayer.
AUTHOR: Mackic J.B.; Stins M.; McComb J.G.; Calero M.; Ghiso J.; Kwang Sik Kim; Shi Du Yan; Stern D.; Schmidt A.M.; Frangione B.; **Zlokovic B.V.**
CORPORATE SOURCE: Dr. B.V. Zlokovic, USC School of Medicine, RMR 506, 2025 Zonal Avenue, Los Angeles, CA 90033, United States. zlokovic@hsc.usc.edu
SOURCE: Journal of Clinical Investigation, (15 Aug 1998) 102/4 (734-743).
Refs: 51
ISSN: 0021-9738 CODEN: JCINAO
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A soluble monomeric form of Alzheimer's amyloid-.beta. (1-40) peptides (SA.beta.1-40) is present in the circulation and could contribute to neurotoxicity if it crosses the brain capillary endothelium, which comprises the blood-brain barrier (BBB) in vivo. This study characterizes endothelial binding and transcytosis of a synthetic peptide homologous to human sA.beta.1- 40 using an in vitro model of human BBB. 125I-sA.beta.1-40 binding to the brain microvascular endothelial cell monolayer was time dependent, polarized to the apical side, and saturable wi'th high- and low-affinity dissociation constants of 7.8.+-.1.2 and 52.8.+-.6.2 nM, respectively. Binding of 125I-sA.beta.1-40 was **inhibited** by anti-**RAGE** (receptor for advanced glycation end products) antibody (63%) and by acetylated low density lipoproteins (33%). Consistent with these data, transfected cultured cells overexpressing **RAGE** or macrophage scavenger receptor (SR), type A, displayed binding and internalization of 125I-sA.beta.1-40. The internalized peptide remains intact > 94%. Transcytosis of 125I-sA.beta.1-40 was time and temperature dependent, asymmetrical from the apical to basolateral side, saturable with a Michaelis constant of 45.+-.9 nM, and partially sensitive to **RAGE** blockade (36%) but not to SR blockade. We conclude that **RAGE** and SR mediate binding of sAB1-40 at the apical side of human BBB, and that **RAGE** is also involved in sA.beta.1-40 transcystosis.

=> d his

(FILE 'HOME' ENTERED AT 10:53:04 ON 22 MAY 2001)

FILE 'EMBASE, CAPLUS, BIOSIS, LIFESCI, MEDLINE' ENTERED AT 10:53:44 ON 22 MAY 2001
L1 3544 S (RECEPTOR FOR ADVANCED GLYCATION ENDPRODUCT) OR (RAGE)
L2 0 S L1 AND (AMYLOID ANGIOPATHY)
L3 108 S L1 AND ALZHEIMER
L4 7 S L3 AND TREAT?
L5 6 DUP REM L4 (1 DUPLICATE REMOVED)
L6 7 S L1 AND VASOCONSTRICT?
L7 3 DUP REM L6 (4 DUPLICATES REMOVED)

L8 115 S L1 AND AMYLOID
L9 6 S L8 AND TREAT?
L10 3 DUP REM L9 (3 DUPLICATES REMOVED)
L11 4 S L1 AND (GENE THERAPY)
L12 4 DUP REM L11 (0 DUPLICATES REMOVED)
L13 398 S L1 AND INHIBIT?
L14 47 S L13 AND SOLUBLE
L15 19 DUP REM L14 (28 DUPLICATES REMOVED)
L16 5 S L13 AND TRANSCYTOSIS
L17 1 DUP REM L16 (4 DUPLICATES REMOVED)
L18 2495 S STERN D?/AU
L19 194 S L1 AND L18
L20 58 S L19 AND INHIBIT?
L21 23 DUP REM L20 (35 DUPLICATES REMOVED)
L22 5704 S SCHMIDT A?/AU
L23 76 S L22 AND L13
L24 34 S L23 AND SOLUBLE
L25 13 DUP REM L24 (21 DUPLICATES REMOVED)
L26 2684 S YAN S?/AU
L27 33 S L13 AND L26
L28 33 S L27 AND INHIBIT?
L29 13 S L28 AND SOLUBLE
L30 4 DUP REM L29 (9 DUPLICATES REMOVED)
L31 549 S ZLOKOVIC B?/AU
L32 10 S L13 AND L31
L33 3 DUP REM L32 (7 DUPLICATES REMOVED)

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	SESSION	TOTAL
FULL ESTIMATED COST		202.89	203.04

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	SESSION	TOTAL
CA SUBSCRIBER PRICE		-17.05	-17.05

STN INTERNATIONAL LOGOFF AT 11:13:58 ON 22 MAY 2001